

WHAT IS CLAIMED IS:

1. A method for producing an infectious, self-replicating, recombinant human parainfluenza virus type 2 (HPIV2) from one or more isolated polynucleotide molecules encoding said HPIV2, comprising:

coexpressing in a cell or cell-free system one or more expression vector(s) comprising a polynucleotide molecule that encodes a partial or complete, polyhexameric recombinant HPIV2 genome or antigenome and one or more polynucleotide molecules encoding PIV N, P and L proteins, thereby producing an infectious HPIV2.

2. The method of claim 1, wherein the HPIV2 genome or antigenome and the N, P, and L proteins are expressed by multiple expression vectors.

3. The method of claim 1, wherein at least one of the N, P and L proteins is supplied by coinfection with PIV.

4. The method of claim 1, wherein the polynucleotide molecule that encodes the recombinant HPIV2 genome or antigenome is cDNA.

5. The method of claim 1, wherein the infectious HPIV2 particle is a complete virus.

6. The method of claim 1, wherein one or more of said N, P and L proteins is/are of a heterologous PIV.

7. The method of claim 1, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome encodes the sequence of a wild-type HPIV2 strain.

8. The method of claim 1, wherein the recombinant HPIV2 genome or antigenome incorporates a recombinantly-introduced restriction site marker or transcriptionally silent point mutation.

9. The method of claim 1, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome incorporates one or more recombinantly-introduced attenuating mutations.

10. The method of claim 1, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome incorporates one or more recombinantly-introduced, temperature sensitive (*ts*) attenuating mutations.

11. The method of claim 1, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome incorporates one or more attenuating mutation(s) identified in a biologically derived mutant PIV strain or other mutant nonsegmented negative stranded RNA virus.

12. The method of claim 11, wherein the recombinant HPIV2 genome or antigenome incorporates one or more attenuating mutations at one or more amino acid position(s) corresponding to an amino acid position of an attenuating mutation identified in a heterologous, mutant nonsegmented negative stranded RNA virus.

13. The method of claim 12, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome incorporates one or more mutation(s) of HPIV3 JS *cp45*.

14. The method of claim 13, wherein the recombinant HPIV2 genome or antigenome incorporates one or more attenuating mutation(s) selected from amino acid substitution(s) or deletion(s) at residues 948 and/or 1566 of the HPIV2 L polymerase.

15. The method of claim 12, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is respiratory syncytial virus (RSV).

16. The method of claim 15, wherein said attenuating mutation comprises an amino acid substitution or deletion at a corresponding target position Phe460 in the HPIV2 L protein.

17. The method of claim 12, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is a bovine parainfluenza virus type 3 (BPIV3).

18. The method of claim 17, wherein said attenuating mutation comprises one or more amino acid substitution(s) or deletion(s) targeting at least Ser1724 in the HPIV2 L protein.

19. The method of claim 18, wherein said attenuating mutation comprises a two amino acid deletion at Ser1724-1725 in the HPIV2 L protein.

20. The method of claim 1, wherein the recombinant HPIV2 genome or antigenome incorporates at least one attenuating mutation stabilized by two or three nucleotide changes in a codon specifying the mutation.

21. The method of claim 1, wherein the recombinant HPIV2 genome or antigenome comprises a nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.

22. The method of claim 21, wherein the nucleotide modification alters one or more HPIV2 N, P, M, F, HN and/or L genes and/or a 3' leader, 5' trailer, and/or intergenic region within the HPIV2 genome or antigenome.

23. The method of claim 21, wherein one or more HPIV2 gene(s) is deleted in whole or in part or expression of the gene(s) is reduced or ablated by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters a translation start site, by introduction of one or more stop codons in an open reading frame (ORF) of the gene, or by a mutation in a transcription signal.

24. The method of claim 21, wherein the recombinant HPIV2 genome or antigenome is modified by a partial or complete deletion of an HPIV2 V open reading frame (ORF), or one or more nucleotide change(s) that reduces or ablates expression of said one HPIV2 V ORF.

25. The method of claim 21, wherein the recombinant HPIV2 genome or antigenome is modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

26. The method of claim 25, wherein the recombinant HPIV2 genome or antigenome is modified to encode a cytokine.

27. The method of claim 1, wherein the recombinant HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome, wherein said vector genome or antigenome is combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s) to form a chimeric HPIV2 genome or antigenome.

28. The method of claim 27, wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are added as supernumerary gene(s) or genome segment(s) adjacent to or within a noncoding region of the partial or complete HPIV2 vector genome or antigenome, or wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are substituted for one or more counterpart gene(s) or genome segment(s) in a partial HPIV2 vector genome or antigenome.

29. The method of claim 27, wherein said one or more heterologous gene(s) or genome segment(s) includes a heterologous regulatory element comprising an extragenic 3' leader or 5' trailer region, a gene-start signal, gene-end signal, editing region, intergenic region, or a 3' or 5' non-coding region.

30. The method of claim 27, wherein said one or more heterologous pathogens is one or more heterologous PIV(s) and said heterologous gene(s) or genome segment(s) encode(s) one or more PIV N, P, V, M, F, HN and/or L protein(s) or fragment(s) thereof.

31. The method of claim 27, wherein the heterologous pathogen is selected from measles virus, subgroup A and subgroup B respiratory syncytial viruses, mumps virus, human papilloma viruses, type 1 and type 2 human immunodeficiency viruses, herpes simplex viruses, cytomegalovirus, rabies virus, Epstein Barr virus, filoviruses, bunyaviruses, flaviviruses, alphaviruses, human metapneumoviruses, and influenza viruses.

32. The method of claim 27, wherein the partial or complete HPIV2 vector genome or antigenome is combined with one or more supernumerary heterologous gene(s) or genome segment(s) to form the chimeric HPIV2 genome or antigenome.

33. The method of claim 32, wherein said one or more supernumerary heterologous gene(s) or genome segment(s) are selected from HPIV1 HN, HPIV2 F, HPIV3 HN, HPIV3 F, and measles HA.

34. The method of claim 27, wherein the HPIV2 vector genome or antigenome incorporates one or more gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of a heterologous HPIV and one or more gene(s) or genome segment(s) encoding one or more heterologous antigenic determinant(s) of a non-PIV pathogen selected from measles virus, respiratory syncytial virus, mumps virus, human papilloma virus, type 1 or type 2 human immunodeficiency virus, herpes simplex virus, cytomegalovirus, rabies virus, Epstein Barr Virus, filovirus, bunyavirus, flavivirus, alphavirus, human metapneumoviruses, and influenza virus.

35. The method of claim 27, wherein the heterologous gene or genome segment is added or substituted at a position corresponding to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete HPIV2 vector genome or antigenome.

36. The method of claim 27, wherein the heterologous gene or genome segment is added or substituted at a position that is more promoter-proximal or promoter-distal compared to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete HPIV2 vector genome or antigenome.

37. The method of claim 27, wherein the HPIV2 vector genome or antigenome is modified to encode a chimeric glycoprotein incorporating one or more heterologous antigenic domains, fragments, or epitopes of a heterologous PIV or non-PIV pathogen to form the chimeric genome or antigenome.

38. The method of claim 37, wherein the HPIV2 vector genome or antigenome is modified to encode a chimeric glycoprotein incorporating one or more antigenic domains, fragments, or epitopes from a second, antigenically distinct PIV to form the chimeric genome or antigenome.

39. The method of claim 37, wherein the chimeric genome or antigenome encodes a chimeric virus or chimeric glycoprotein having antigenic domains, fragments, or epitopes from two or more HPIVs.

40. The method of claim 37, wherein the heterologous genome segment encodes a glycoprotein cytoplasmic, transmembrane or ectodomain which is substituted for a corresponding glycoprotein domain in the HPIV2 vector genome or antigenome.

41. The method of claim 37, wherein one or more heterologous genome segment(s) of a second, antigenically distinct HPIV encoding said one or more antigenic domains, fragments, or epitopes is/are substituted within a HPIV2 vector genome or antigenome to encode said chimeric glycoprotein.

42. The method of claim 37, wherein said one or more heterologous genome segment(s) are selected from ectodomains of HPIV1 and/or HPIV3 HN and/or F glycoproteins.

43. The method of claim 27, wherein the chimeric HPIV2 genome or antigenome is modified by introduction of one or more attenuating mutations identified in a biologically derived mutant PIV or other mutant nonsegmented negative stranded RNA virus.

44. The method of claim 43, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome incorporates one or more mutation(s) of HPIV3 JS *cp45*.

45. The method of claim 44, wherein the recombinant HPIV2 genome or antigenome incorporates one or more attenuating mutation(s) selected from amino acid substitution(s) or deletion(s) at residues 948 and/or 1566 of the HPIV2 L polymerase.

46. The method of claim 43, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is respiratory syncytial virus (RSV).

47. The method of claim 46, wherein said attenuating mutation comprises an amino acid substitution or deletion at a corresponding target position Phe460 in the HPIV2 L protein.

48. The method of claim 43, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is a bovine parainfluenza virus type 3 (BPIV3).

49. The method of claim 48, wherein said attenuating mutation comprises one or more amino acid substitution(s) or deletion(s) targeting at least Ser1724 in the HPIV2 L protein.

50. The method of claim 49, wherein said attenuating mutation comprises a two amino acid deletion at Ser1724-1725 in the HPIV2 L protein.

51. The method of claim 43, wherein the chimeric HPIV2 genome or antigenome incorporates at least one attenuating mutation stabilized by two or three nucleotide changes in a codon specifying the mutation.

52. The method of claim 43, wherein said one or combination of mutation(s) in the chimeric HPIV2 genome or antigenome is/are located in the partial or complete HPIV2 vector genome or antigenome.

53. The method of claim 41, wherein said one or more attenuating mutations is/are located in the heterologous gene(s) or genome segment(s) incorporated in the chimeric genome or antigenome.

54. The method of claim 27, wherein the chimeric HPIV2 genome or antigenome is further modified to incorporate an additional nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.

55. The method of claim 54, wherein the chimeric HPIV2 genome or antigenome is further modified such that one or more HPIV2 gene(s) is/are deleted in whole or in part or expression of the gene(s) is reduced or ablated by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters a translation start site, by introduction of one or more stop codons in an open reading frame (ORF) of the gene, or by a mutation in a transcription signal.

56. The method of claim 55, wherein the chimeric HPIV2 genome or antigenome is modified by a partial or complete deletion of an HPIV2 V open reading frame (ORF) or by one or more nucleotide change(s) that reduces or ablates expression of said HPIV2 V ORF.

57. The method of claim 54, wherein the chimeric HPIV2 genome or antigenome is further modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

58. The method of claim 27, wherein the chimeric HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous genes or genome segments from a bovine parainfluenza virus type 3 virus (BPIV3) to form a human-bovine chimeric HPIV2 genome or antigenome.

59. The method of claim 58, wherein the partial or complete HPIV2 vector genome or antigenome is combined with one or more heterologous gene(s) or genome segment(s) of a N, P, L, or M gene of a BPIV3 to form a human-bovine chimeric genome or antigenome.

60. The method of claim 58, wherein a bovine PIV (BPIV) N, M, L, or P open reading frame (ORF) or a genome segment thereof is substituted for a counterpart HPIV2 N, M, L, or P ORF or genome segment to form a chimeric HPIV2-BPIV3 genome or antigenome.

61. The method of claim 27, wherein the chimeric HPIV2 genome or antigenome is modified by addition or substitution of one or more additional heterologous gene(s) or genome segment(s) from a bovine parainfluenza virus type 3 virus (BPIV3) within the partial or complete HPIV2 vector genome or antigenome to increase genetic stability or alter attenuation, reactogenicity or growth in culture of the recombinant virus.

62. The method of claim 27, wherein the chimeric HPIV2 genome or antigenome incorporates a polynucleotide insertion of between 150 nucleotides (nts) and 4,000 nucleotides in length in a non-coding region (NCR) of the genome or antigenome or as a separate gene unit (GU), said polynucleotide insertion lacking a complete open reading frame (ORF) and specifying an attenuated phenotype in said recombinant HPIV2.

63. The method of claim 62, wherein said polynucleotide insert is introduced into the HPIV2 genome or antigenome in a reverse, non-sense orientation whereby the insert does not encode protein.

64. The method of claim 62, wherein said recombinant HPIV2 replicates efficiently *in vitro* and exhibits an attenuated phenotype *in vivo*.

65. The method of claim 62, wherein said polynucleotide insertion adds a total length of foreign sequence to the recombinant HPIV2 genome or antigenome of 30% to 50% or greater compared to a wild-type HPIV2 genome length.

66. The method of claim 62, wherein said polynucleotide insertion specifies an attenuation phenotype of the recombinant HPIV2 which exhibits at least a 10-to 100-fold decrease in replication in the upper and/or lower respiratory tract.

67. An isolated, infectious, self-replicating, recombinant human parainfluenza virus type 2 (HPIV2) comprising a PIV major nucleocapsid (N) protein, a PIV nucleocapsid phosphoprotein (P), a PIV large polymerase protein (L), and a partial or complete, polyhexameric recombinant HPIV2 genome or antigenome.

68. The recombinant HPIV2 of claim 67, wherein at least one of the N, P and L proteins is of a different HPIV or a bovine parainfluenza virus type 3 virus (BPIV3).

69. The recombinant HPIV2 of claim 67, wherein one or more of said N, P and L proteins is/are of HPIV3.

70. The recombinant HPIV2 of claim 67, wherein the recombinant HPIV2 genome or antigenome is encoded by cDNA.

71. The recombinant HPIV2 of claim 67, wherein the infectious HPIV2 particle is a complete virus.

72. The recombinant HPIV2 of claim 67, wherein the recombinant HPIV2 genome or antigenome is of a wild-type HPIV2 strain.

73. The recombinant HPIV2 of claim 67, wherein the recombinant HPIV2 genome or antigenome incorporates one or more recombinantly-introduced attenuating mutations.

74. The recombinant HPIV2 of claim 67, wherein the recombinant HPIV2 genome or antigenome incorporates one or more recombinantly-introduced attenuating mutations at one or more amino acid position(s) corresponding to an amino acid position of an attenuating mutation identified in a heterologous, mutant nonsegmented negative stranded RNA virus.

75. The recombinant HPIV2 of claim 74, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome incorporates one or more mutation(s) of HPIV3 JS *cp45*.

76. The recombinant HPIV2 of claim 75, wherein the recombinant HPIV2 genome or antigenome incorporates one or more attenuating mutation(s) selected from amino acid substitution(s) or deletion(s) at residues 948 and/or 1566 of the HPIV2 L polymerase.

77. The recombinant HPIV2 of claim 74, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is respiratory syncytial virus (RSV).

78. The recombinant HPIV2 of claim 77, wherein said attenuating mutation comprises an amino acid substitution or deletion at a corresponding target position Phe460 in the HPIV2 L protein.

79. The recombinant HPIV2 of claim 74, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is a bovine parainfluenza virus type 3 (BPIV3).

80. The recombinant HPIV2 of claim 79, wherein said attenuating mutation comprises one or more amino acid substitution(s) or deletion(s) targeting at least Ser1724 in the HPIV2 L protein.

81. The recombinant HPIV2 of claim 80, wherein said attenuating mutation comprises a two amino acid deletion at Ser1724-1725 in the HPIV2 L protein.

82. The recombinant HPIV2 of claim 74, wherein the recombinant HPIV2 genome or antigenome incorporates at least one attenuating mutation stabilized by two or three nucleotide changes in a codon specifying the mutation.

83. The recombinant HPIV2 of claim 67, wherein the recombinant HPIV2 genome or antigenome comprises a nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.

84. The recombinant HPIV2 of claim 83, wherein the additional nucleotide modification alters one or more HPIV2 N, P, M, F, HN and/or L genes and/or a 3' leader, 5' trailer, and/or intergenic region within the HPIV2 genome or antigenome.

85. The recombinant HPIV2 of claim 83, wherein one or more HPIV2 gene(s) is deleted in whole or in part or expression of the gene(s) is reduced or ablated by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters a translation start site, by introduction of one or more stop codons in an open reading frame (ORF) of the gene, or by a mutation in a transcription signal.

86. The recombinant HPIV2 of claim 85, wherein the recombinant HPIV2 genome or antigenome is modified by a partial or complete deletion of an HPIV2 V open reading frame (ORF), or one or more nucleotide change(s) that reduces or ablates expression of said one HPIV2 V ORF.

87. The recombinant HPIV2 of claim 83, wherein the recombinant HPIV2 genome or antigenome is modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

88. The recombinant HPIV2 of claim 87, wherein the recombinant HPIV2 genome or antigenome is modified to encode a cytokine.

89. The recombinant HPIV2 of claim 67, wherein the recombinant HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome, wherein said vector genome or antigenome is combined with one or more heterologous

gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s) to form a chimeric HPIV2 genome or antigenome.

90. The recombinant HPIV2 of claim 89, wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are added as supernumerary gene(s) or genome segment(s) adjacent to or within a noncoding region of the partial or complete HPIV2 vector genome or antigenome, or wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are substituted for one or more counterpart gene(s) or genome segment(s) in a partial HPIV2 vector genome or antigenome.

91. The recombinant HPIV2 of claim 89, wherein said one or more heterologous gene(s) or genome segment(s) includes a heterologous regulatory element comprising an extragenic 3' leader or 5' trailer region, a gene-start signal, gene-end signal, editing region, intergenic region, or a 3' or 5' non-coding region.

92. The recombinant HPIV2 of claim 89, wherein said one or more heterologous pathogens is/are one or more heterologous PIV(s) and said heterologous gene(s) or genome segment(s) encode(s) one or more PIV N, P, V, M, F, HN and/or L protein(s) or fragment(s) thereof.

93. The recombinant HPIV2 of claim 89, wherein the heterologous pathogen is selected from measles virus, subgroup A and subgroup B respiratory syncytial viruses, mumps virus, human papilloma viruses, type 1 and type 2 human immunodeficiency viruses, herpes simplex viruses, cytomegalovirus, rabies virus, Epstein Barr virus, filoviruses, bunyaviruses, flaviviruses, alphaviruses, human metapneumoviruses, and influenza viruses.

94. The recombinant HPIV2 of claim 89, wherein the partial or complete HPIV2 vector genome or antigenome is combined with one or more supernumerary heterologous gene(s) or genome segment(s) to form the chimeric HPIV2 genome or antigenome.

95. The recombinant HPIV2 of claim 94, wherein said one or more supernumerary heterologous gene(s) or genome segment(s) are selected from HPIV1 HN, HPIV2 F, HPIV3 HN, HPIV3 F, and measles HA.

96. The recombinant HPIV2 of claim 89, wherein the HPIV2 vector genome or antigenome incorporates one or more gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of a heterologous HPIV and one or more gene(s) or genome segment(s) encoding one or more heterologous antigenic determinant(s) of a non-PIV pathogen selected from measles virus, respiratory syncytial virus (RSV), mumps virus, human papilloma virus, type 1 or type 2 human immunodeficiency virus, herpes simplex virus, cytomegalovirus, rabies virus, Epstein Barr Virus, filovirus, bunyavirus, flavivirus, alphavirus, human metapneumoviruses, and influenza virus.

97. The recombinant HPIV2 of claim 96, wherein the heterologous pathogen is RSV and the heterologous antigenic determinant(s) is/are selected from the RSV G and F proteins and antigenic domains, fragments and epitopes thereof.

98. The recombinant HPIV2 of claim 89, wherein the heterologous gene or genome segment is added or substituted at a position corresponding to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete HPIV2 vector genome or antigenome.

99. The recombinant HPIV2 of claim 89, wherein the heterologous gene or genome segment is added or substituted at a position that is more promoter-proximal or promoter-distal compared to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete HPIV2 vector genome or antigenome.

100. The recombinant HPIV2 of claim 89, wherein the HPIV2 vector genome or antigenome is modified to encode a chimeric glycoprotein incorporating one or more heterologous antigenic domains, fragments, or epitopes of a heterologous PIV or non-PIV pathogen to form the chimeric genome or antigenome.

101. The recombinant HPIV2 of claim 100, wherein the HPIV2 vector genome or antigenome is modified to encode a chimeric glycoprotein incorporating one or more antigenic domains, fragments, or epitopes from a second, antigenically distinct PIV to form the chimeric genome or antigenome.

102. The recombinant HPIV2 of claim 101, wherein the chimeric genome or antigenome encodes a chimeric virus or chimeric glycoprotein having antigenic domains, fragments, or epitopes from two or more HPIVs.

103. The recombinant HPIV2 of claim 100, wherein the heterologous genome segment encodes a glycoprotein cytoplasmic, transmembrane or ectodomain which is substituted for a corresponding glycoprotein domain in the HPIV2 vector genome or antigenome.

104. The recombinant HPIV2 of claim 100, wherein said one or more heterologous genome segment(s) are selected from ectodomains of HPIV1 and/or HPIV3 HN and/or F glycoproteins.

105. The recombinant HPIV2 of claim 89, wherein the chimeric HPIV2 genome or antigenome incorporates one or more recombinantly-introduced attenuating mutations at one or more amino acid position(s) corresponding to an amino acid position of an attenuating mutation identified in a heterologous, mutant nonsegmented negative stranded RNA virus.

106. The recombinant HPIV2 of claim 105, wherein the polynucleotide molecule encoding the chimeric HPIV2 genome or antigenome incorporates one or more mutation(s) of HPIV3 JS *cp45*.

107. The recombinant HPIV2 of claim 106, wherein the chimeric HPIV2 genome or antigenome incorporates one or more attenuating mutation(s) selected from amino acid substitution(s) or deletion(s) at residues 948 and/or 1566 of the HPIV2 L polymerase.

108. The recombinant HPIV2 of claim 105, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is respiratory syncytial virus (RSV).

109. The recombinant HPIV2 of claim 108, wherein said attenuating mutation comprises an amino acid substitution or deletion at a corresponding target position Phe460 in the HPIV2 L protein.

110. The recombinant HPIV2 of claim 105, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is a bovine parainfluenza virus type 3 (BPIV3).

111. The recombinant HPIV2 of claim 110, wherein said attenuating mutation comprises one or more amino acid substitution(s) or deletion(s) targeting at least Ser1724 in the HPIV2 L protein.

112. The recombinant HPIV2 of claim 111, wherein said attenuating mutation comprises a two amino acid deletion at Ser1724-1725 in the HPIV2 L protein.

113. The recombinant HPIV2 of claim 105, wherein the recombinant HPIV2 genome or antigenome incorporates at least one attenuating mutation stabilized by two or three nucleotide changes in a codon specifying the mutation.

114. The recombinant HPIV2 of claim 105, wherein said one or more mutation(s) in the chimeric HPIV2 genome or antigenome is/are located in the partial or complete HPIV2 vector genome or antigenome.

115. The recombinant HPIV2 of claim 114, wherein said one or more mutation(s) in the chimeric HPIV1 genome or antigenome is/are located in the heterologous gene(s) or genome segment(s) incorporated in the chimeric genome or antigenome.

116. The recombinant HPIV2 of claim 89, wherein the chimeric HPIV2 genome or antigenome is modified to incorporate an additional nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.

117. The recombinant HPIV2 of claim 116, wherein the chimeric HPIV2 genome or antigenome is modified such that one or more HPIV2 gene(s) is/are deleted in whole or in part or expression of the gene(s) is reduced or ablated by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters a translation start site, by introduction of one or more stop codons in an open reading frame (ORF) of the gene, or by a mutation in a transcription signal.

118. The recombinant HPIV2 of claim 117, wherein the chimeric HPIV2 genome or antigenome is modified by a partial or complete deletion of an HPIV2 V open reading frame (ORF) or by one or more nucleotide change(s) that reduces or ablates expression of said HPIV2 V ORF.

119. The recombinant HPIV2 of claim 116, wherein the chimeric HPIV2 genome or antigenome is further modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

120. The recombinant HPIV2 of claim 89, wherein the chimeric HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous genes or genome segments from a bovine parainfluenza virus type 3 virus (BPIV3) to form a human-bovine chimeric HPIV2 genome or antigenome.

121. The recombinant HPIV2 of claim 120, wherein the partial or complete HPIV2 vector genome or antigenome is combined with one or more heterologous gene(s) or genome segment(s) of a N, P, L, or M gene of a BPIV3 to form a human-bovine chimeric genome or antigenome.

122. The recombinant HPIV2 of claim 120, wherein a BPIV3 N, M, L, or P open reading frame (ORF) or a genome segment thereof is substituted for a counterpart HPIV2 N, M, L, or P ORF or genome segment to form a chimeric HPIV2-BPIV3 genome or antigenome.

123. The recombinant HPIV2 of claim 89, wherein the chimeric HPIV2 genome or antigenome is further modified by addition or substitution of one or more additional heterologous gene(s) or genome segment(s) from a bovine parainfluenza virus type 3 virus (BPIV3) within the partial or complete HPIV2 vector genome or antigenome to increase genetic stability or alter attenuation, reactogenicity or growth in culture of the recombinant virus.

124. The recombinant HPIV2 of claim 67, wherein the recombinant HPIV2 genome or antigenome incorporates a polynucleotide insertion of between 150 nucleotides (nts) and 4,000 nucleotides in length in a non-coding region (NCR) of the genome or antigenome or as a separate gene unit (GU), said polynucleotide insertion lacking a complete open reading frame (ORF) and specifying an attenuated phenotype in said recombinant HPIV2.

125. The recombinant HPIV2 of claim 124, wherein said polynucleotide insert is introduced into the HPIV2 genome or antigenome in a reverse, non-sense orientation whereby the insert does not encode protein.

126. The recombinant HPIV2 of claim 124, wherein said recombinant HPIV2 replicates efficiently *in vitro* and exhibits an attenuated phenotype *in vivo*.

127. The recombinant HPIV2 of claim 124, wherein said polynucleotide insertion adds a total length of foreign sequence to the recombinant HPIV2 genome or antigenome of 30% to 50% or greater compared to a wild-type HPIV2 genome length.

128. The recombinant HPIV2 of claim 124, wherein said polynucleotide insertion specifies an attenuation phenotype of the recombinant HPIV2 which exhibits at least a 10-to 100-fold decrease in replication in the upper and/or lower respiratory tract. wherein one or more of the PIV N, P, and/or L proteins are of a heterologous PIV.

129. An immunogenic composition comprising an immunogenically effective amount of an isolated, infectious, self-replicating, recombinant human parainfluenza virus type 2 (HPIV2) in a pharmaceutically acceptable carrier, said HPIV2 comprising a polyhexameric, recombinant HPIV2 genome or antigenome, a PIV N protein, a PIV P protein, and a PIV L protein.

130. The immunogenic composition of claim 129, wherein one or more of the PIV N, P, and/or L proteins are of a heterologous PIV.

131. The immunogenic composition of claim 129, wherein the recombinant HPIV2 is a complete virus.

132. The immunogenic composition of claim 129, wherein the recombinant HPIV2 genome or antigenome comprises the sequence of a wild-type HPIV2 strain.

133. The immunogenic composition of claim 129, wherein the recombinant HPIV2 genome or antigenome incorporates one or more recombinantly-introduced attenuating mutations.

134. The immunogenic composition of claim 133, wherein the recombinant HPIV2 genome or antigenome incorporates one or more recombinantly-introduced attenuating mutations at one or more amino acid position(s) corresponding to an amino acid position of an attenuating mutation identified in a heterologous, mutant nonsegmented negative stranded RNA virus.

135. The immunogenic composition of claim 134, wherein the recombinant HPIV2 genome or antigenome incorporates one or more mutation(s) of HPIV3 JS *cp45*.

136. The immunogenic composition of claim 135, wherein the recombinant HPIV2 genome or antigenome incorporates one or more attenuating mutation(s) selected from amino acid substitution(s) or deletion(s) at residues 948 and/or 1566 of the HPIV2 L polymerase.

137. The immunogenic composition of claim 134, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is respiratory syncytial virus (RSV).

138. The immunogenic composition of claim 137, wherein said attenuating mutation comprises an amino acid substitution or deletion at a corresponding target position Phe460 in the HPIV2 L protein.

139. The immunogenic composition of claim 134, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is a bovine parainfluenza virus type 3 (BPIV3).

140. The immunogenic composition of claim 139, wherein said attenuating mutation comprises one or more amino acid substitution(s) or deletion(s) targeting at least Ser1724 in the HPIV2 L protein.

141. The immunogenic composition of claim 140, wherein said attenuating mutation comprises a two amino acid deletion at Ser1724-1725 in the HPIV2 L protein.

142. The immunogenic composition of claim 134, wherein the recombinant HPIV2 genome or antigenome incorporates at least one attenuating mutation stabilized by two or three nucleotide changes in a codon specifying the mutation.

143. The immunogenic composition of claim 134, wherein said one or more mutations specify one or more change(s) in a HPIV2 L, M, N, P, F, or HN gene and/or in a HPIV2 extragenic sequence.

144. The immunogenic composition of claim 134, wherein said attenuating mutation comprises three nucleotide changes in a codon specifying the mutation.

145. The immunogenic composition of claim 129, wherein the recombinant HPIV2 genome or antigenome comprises a nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.

146. The immunogenic composition of claim 145, wherein the nucleotide modification alters one or more HPIV2 N, P, M, F, HN and/or L genes and/or a 3' leader, 5' trailer, and/or intergenic region within the HPIV2 genome or antigenome.

147. The immunogenic composition of claim 146, wherein one or more HPIV2 gene(s) is deleted in whole or in part or expression of the gene(s) is reduced or ablated by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters a translation start site, by introduction of one or more stop codons in an open reading frame (ORF) of the gene, or by a mutation in a transcription signal.

148. The immunogenic composition of claim 147, wherein the recombinant HPIV2 genome or antigenome is modified by a partial or complete deletion of an HPIV2 V open reading frame (ORF), or one or more nucleotide change(s) that reduces or ablates expression of said HPIV2 V ORF.

149. The immunogenic composition of claim 145, wherein the recombinant HPIV2 genome or antigenome is modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

150. The immunogenic composition of claim 145, wherein the recombinant HPIV2 genome or antigenome is modified to encode a cytokine.

151. The immunogenic composition of claim 129, wherein the recombinant HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome, wherein said vector genome or antigenome is combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s) to form a chimeric HPIV2 genome or antigenome.

152. The immunogenic composition of claim 151, wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are added as supernumerary gene(s) or genome segment(s) adjacent to or within a noncoding region of the partial or complete HPIV2 vector genome or antigenome, or wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are substituted for one or more counterpart gene(s) or genome segment(s) in a partial HPIV2 vector genome or antigenome.

153. The immunogenic composition of claim 151, wherein said one or more heterologous gene(s) or genome segment(s) includes a heterologous regulatory element comprising an extragenic 3' leader or 5' trailer region, a gene-start signal, gene-end signal, editing region, intergenic region, or a 3' or 5' non-coding region.

154. The immunogenic composition of claim 151, wherein said one or more heterologous pathogens is/are one or more heterologous PIV(s) and said heterologous gene(s) or genome segment(s) encode(s) one or more PIV N, P, V, M, F, HN and/or L protein(s) or fragment(s) thereof.

155. The immunogenic composition of claim 151, wherein the heterologous pathogen is selected from measles virus, subgroup A and subgroup B respiratory syncytial viruses, mumps virus, human papilloma viruses, type 1 and type 2 human immunodeficiency viruses, herpes simplex viruses, cytomegalovirus, rabies virus, Epstein Barr virus, filoviruses, bunyaviruses, flaviviruses, alphaviruses, human metapneumoviruses, and influenza viruses.

156. The immunogenic composition of claim 151, wherein the partial or complete HPIV2 vector genome or antigenome is combined with one or more supernumerary heterologous gene(s) or genome segment(s) to form the chimeric HPIV2 genome or antigenome.

157. The immunogenic composition of claim 151, wherein the HPIV2 vector genome or antigenome incorporates one or more gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of a heterologous HPIV and one or more gene(s) or genome segment(s) encoding one or more heterologous antigenic determinant(s) of a non-PIV pathogen selected from measles virus, respiratory syncytial virus, mumps virus, human papilloma virus, type 1 or type 2 human immunodeficiency virus, herpes simplex virus, cytomegalovirus, rabies virus, Epstein Barr Virus, filovirus, bunyavirus, flavivirus, alphavirus, human metapneumoviruses, and influenza virus.

158. The immunogenic composition of claim 151, wherein the heterologous gene or genome segment is added or substituted at a position corresponding to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete HPIV2 vector genome or antigenome or, alternatively, at a position that is more promoter-proximal or promoter-distal compared to a wild-type gene order position of the counterpart gene or genome segment within the partial or complete HPIV2 vector genome or antigenome.

159. The immunogenic composition of claim 151, wherein the HPIV2 vector genome or antigenome is modified to encode a chimeric glycoprotein incorporating one or more heterologous antigenic domains, fragments, or epitopes of a heterologous PIV or non-PIV pathogen to form the chimeric genome or antigenome.

160. The immunogenic composition of claim 151, wherein the chimeric HPIV2 genome or antigenome comprises one or more recombinantly-introduced attenuating mutations.

161. The immunogenic composition of claim 160, wherein the recombinant HPIV2 genome or antigenome incorporates one or more recombinantly-introduced attenuating mutations at one or more amino acid position(s) corresponding to an amino acid position of an attenuating mutation identified in a heterologous, mutant nonsegmented negative stranded RNA virus.

162. The immunogenic composition of claim 161, wherein the recombinant HPIV2 genome or antigenome incorporates one or more mutation(s) of HPIV3 JS *cp45*.

163. The immunogenic composition of claim 162, wherein the recombinant HPIV2 genome or antigenome incorporates one or more attenuating mutation(s) selected from amino acid substitution(s) or deletion(s) at residues 948 and/or 1566 of the HPIV2 L polymerase.

164. The immunogenic composition of claim 161, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is respiratory syncytial virus (RSV).

165. The immunogenic composition of claim 164, wherein said attenuating mutation comprises an amino acid substitution or deletion at a corresponding target position Phe460 in the HPIV2 L protein.

166. The immunogenic composition of claim 161, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is a bovine parainfluenza virus type 3 (BPIV3).

167. The immunogenic composition of claim 166, wherein said attenuating mutation comprises one or more amino acid substitution(s) or deletion(s) targeting at least Ser1724 in the HPIV2 L protein.

168. The immunogenic composition of claim 167, wherein said attenuating mutation comprises a two amino acid deletion at Ser1724-1725 in the HPIV2 L protein.

169. The immunogenic composition of claim 160, wherein the recombinant HPIV2 genome or antigenome incorporates at least one attenuating mutation stabilized by two or three nucleotide changes in a codon specifying the mutation.

170. The immunogenic composition of claim 160, wherein said one or more mutations specify one or more change(s) in a HPIV2 L, M, N, P, F, or HN gene and/or in a HPIV2 extragenic sequence.

171. The immunogenic composition of claim 160, wherein said attenuating mutation comprises three nucleotide changes in a codon specifying the mutation.

172. The immunogenic composition of claim 151, wherein the chimeric HPIV2 genome or antigenome is modified to incorporate a nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-

sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.

173. The immunogenic composition of claim 172, wherein the chimeric HPIV2 genome or antigenome is modified such that one or more HPIV2 gene(s) is/are deleted in whole or in part or expression of the gene(s) is reduced or ablated by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters a translation start site, by introduction of one or more stop codons in an open reading frame (ORF) of the gene, or by a mutation in a transcription signal.

174. The immunogenic composition of claim 172, wherein the chimeric HPIV2 genome or antigenome is modified by a partial or complete deletion of an HPIV2 V open reading frame (ORF) or by one or more nucleotide change(s) that reduces or ablates expression of said HPIV2 V ORF.

175. The immunogenic composition of claim 172, wherein the chimeric HPIV2 genome or antigenome is further modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

176. The immunogenic composition of claim 172, wherein the recombinant HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous genes or genome segments from a bovine parainfluenza virus (BPIV) to form a human-bovine chimeric HPIV2 genome or antigenome.

177. The immunogenic composition of claim 172, wherein the partial or complete HPIV2 vector genome or antigenome is combined with one or more heterologous gene(s) or genome segment(s) of a N, P, L, or M gene of a BPIV to form a human-bovine chimeric genome or antigenome.

178. The immunogenic composition of claim 129, wherein the recombinant HPIV2 genome or antigenome incorporates a polynucleotide insertion of between 150 nucleotides (nts) and 4,000 nucleotides in length in a non-coding region (NCR) of the genome or antigenome or as a separate gene unit (GU), said polynucleotide insertion lacking a complete

open reading frame (ORF) and specifying an attenuated phenotype in said recombinant HPIV2.

179. The immunogenic composition of claim 178, wherein said polynucleotide insertion specifies an attenuation phenotype of the recombinant HPIV2 which exhibits at least a 10-to 100-fold decrease in replication in the upper and/or lower respiratory tract.

180. The immunogenic composition of claim 129, wherein the recombinant HPIV2 is formulated in a dose of 10^3 to 10^7 PFU.

181. The immunogenic composition of claim 129, wherein the recombinant HPIV2 is formulated for administration to the upper respiratory tract.

182. The immunogenic composition of claim 129, wherein the recombinant HPIV2 is formulated for administration by spray, droplet or aerosol.

183. A method for stimulating the immune system of a mammalian subject to induce an immune response in the subject against PIV which comprises administering to the subject an immunologically sufficient amount of an isolated, infectious, self-replicating, recombinant human parainfluenza virus type 2 (HPIV2) comprising a PIV major nucleocapsid (N) protein, a PIV nucleocapsid phosphoprotein (P), a PIV large polymerase protein (L), and a partial or complete, polyhexameric recombinant HPIV2 genome or antigenome.

184. The method of claim 183, wherein the recombinant HPIV2 is administered in a dose of 10^3 to 10^7 PFU.

185. The method of claim 183, wherein the recombinant HPIV2 is administered to the upper respiratory tract.

186. The method of claim 183, wherein the recombinant HPIV2 is administered by spray, droplet or aerosol.

187. The method of claim 183, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome incorporates one or more recombinantly-introduced attenuating mutations.

188. The method of claim 187, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome incorporates one or more attenuating mutation(s) identified in a biologically derived mutant PIV strain or other mutant nonsegmented negative stranded RNA virus.

189. The method of claim 188, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome incorporates one or any combination of mutation(s) selected from mutations specifying amino acid substitution(s) or deletion(s) at corresponding target position(s) Tyr948, Ala998, Leu1566, Phe460 and/or Ser1724 in the HPIV2 L protein.

190. The method of claim 183, wherein the recombinant HPIV2 genome or antigenome incorporates at least one attenuating mutation stabilized by two or three nucleotide changes in a codon specifying the mutation.

191. The method of claim 190, wherein said attenuating mutation comprises three nucleotide changes in a codon specifying an amino acid substitution or deletion at Ser1724 in the HPIV2 L protein.

192. The method of claim 183, wherein the recombinant HPIV2 genome or antigenome is incorporates a nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.

193. The method of claim 192, wherein the nucleotide modification alters one or more HPIV2 N, P, M, F, HN and/or L genes and/or a 3' leader, 5' trailer, and/or intergenic region within the HPIV2 genome or antigenome.

194. The method of claim 192, wherein the recombinant HPIV2 genome or antigenome is modified such that one or more HPIV2 gene(s) is/are deleted in whole or in part or expression of the gene(s) is reduced or ablated by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters a translation start site, by introduction of one or more stop codons in an open reading frame (ORF) of the gene, or by a mutation in a transcription signal.

195. The method of claim 194, wherein the recombinant HPIV2 genome or antigenome is modified by a partial or complete deletion of an HPIV2 V open reading frame (ORF) or by one or more nucleotide change(s) that reduces or ablates expression of said HPIV2 V ORF.

196. The method of claim 192, wherein the recombinant HPIV2 genome or antigenome is further modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

197. The method of claim 183, wherein the recombinant HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous genes or genome segments from a bovine parainfluenza virus type 3 virus (BPIV3) to form a human-bovine chimeric HPIV2 genome or antigenome.

198. The method of claim 197, wherein the partial or complete HPIV2 vector genome or antigenome is combined with one or more heterologous gene(s) or genome segment(s) of a N, P, L, or M gene of a BPIV3 to form a human-bovine chimeric genome or antigenome.

199. The method of claim 183, wherein the recombinant HPIV2 genome or antigenome incorporates a polynucleotide insertion of between 150 nucleotides (nts) and 4,000 nucleotides in length in a non-coding region (NCR) of the genome or antigenome or as a separate gene unit (GU), said polynucleotide insertion lacking a complete open reading frame (ORF) and specifying an attenuated phenotype in said recombinant HPIV2.

200. The method of claim 199, wherein said polynucleotide insertion specifies an attenuation phenotype of the recombinant HPIV2 which exhibits at least a 10-to 100-fold decrease in replication in the upper and/or lower respiratory tract.

201. The method of claim 183, wherein the recombinant HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome and said vector genome or antigenome is combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s) to form a chimeric HPIV2 genome or antigenome.

202. The method of claim 201, wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are added as supernumerary gene(s) or genome segment(s) adjacent to or within a noncoding region of the partial or complete HPIV2 vector genome or antigenome, or wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are substituted for one or more counterpart gene(s) or genome segment(s) in a partial HPIV2 vector genome or antigenome.

203. The method of claim 201, wherein said one or more heterologous pathogens is one or more heterologous PIV(s) and said heterologous gene(s) or genome segment(s) encode(s) one or more PIV N, P, V, M, F, HN and/or L protein(s) or fragment(s) thereof.

204. The method of claim 201, wherein the heterologous pathogen is selected from measles virus, subgroup A and subgroup B respiratory syncytial viruses, mumps virus, human papilloma viruses, type 1 and type 2 human immunodeficiency viruses, herpes simplex viruses, cytomegalovirus, rabies virus, Epstein Barr virus, filoviruses, bunyaviruses, flaviviruses, alphaviruses, human metapneumoviruses, and influenza viruses.

205. The method of claim 201, wherein the chimeric HPIV2 genome or antigenome incorporates one or more gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of a heterologous HPIV and one or more gene(s) or genome segment(s) encoding one or more heterologous antigenic determinant(s) of a non-PIV pathogen selected from measles virus, respiratory syncytial virus, mumps virus, human papilloma virus, type 1 or type 2 human immunodeficiency virus, herpes simplex virus, cytomegalovirus, rabies virus, Epstein Barr Virus, filovirus, bunyavirus, flavivirus, human metapneumoviruses, alphavirus and influenza virus.

206. The method of claim 201, wherein the chimeric HPIV2 genome or antigenome encodes a chimeric virus or chimeric glycoprotein having antigenic domains, fragments, or epitopes from two or more HPIVs.

207. The method of claim 201, wherein the chimeric HPIV2 genome or antigenome is modified by introduction of one or more attenuating mutations.

208. The method of claim 201, wherein the chimeric HPIV2 genome or antigenome further comprises one or more attenuating mutations identified in a biologically derived mutant PIV or other mutant nonsegmented negative stranded RNA virus.

209. The method of claim 208, wherein the chimeric HPIV2 genome or antigenome incorporates one or any combination of mutation(s) selected from mutations specifying amino acid substitution(s) or deletion(s) at corresponding target position(s) Tyr948, Ala998, Leu1566, Phe460 and/or Ser1724 in the HPIV2 L protein.

210. The method of claim 201, wherein the chimeric HPIV2 genome or antigenome incorporates at least one attenuating mutation stabilized by two or three nucleotide changes in a codon specifying the mutation.

211. The method of claim 210, wherein said attenuating mutation comprises three nucleotide changes in a codon specifying the mutation.

212. The method of claim 201, wherein the chimeric HPIV2 genome or antigenome is modified to incorporate an additional nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.

213. The method of claim 201, wherein the chimeric HPIV2 genome or antigenome is further modified such that one or more HPIV2 gene(s) is/are deleted in whole or in part or expression of the gene(s) is reduced or ablated by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters a translation start site, by introduction of one or more stop codons in an open reading frame (ORF) of the gene, or by a mutation in a transcription signal.

214. The method of claim 201, wherein the chimeric HPIV2 genome or antigenome is modified by a partial or complete deletion of an HPIV2 V open reading frame (ORF) or by one or more nucleotide change(s) that reduces or ablates expression of said HPIV2 V ORF.

215. The method of claim 201, wherein the chimeric HPIV2 genome or antigenome is further modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

216. The method of claim 183, wherein the recombinant HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous genes or genome segments from a bovine parainfluenza type 3 virus (BPIV3) to form a human-bovine chimeric HPIV2 genome or antigenome.

217. The method of claim 183, wherein the partial or complete HPIV2 vector genome or antigenome is combined with one or more heterologous gene(s) or genome segment(s) of a N, P, L, or M gene of a BPIV3 to form a human-bovine chimeric genome or antigenome.

218. The method of claim 183, wherein the recombinant HPIV2 genome or antigenome incorporates a polynucleotide insertion of between 150 nucleotides (nts) and 4,000 nucleotides in length in a non-coding region (NCR) of the genome or antigenome or as a separate gene unit (GU), said polynucleotide insertion lacking a complete open reading frame (ORF) and specifying an attenuated phenotype in said recombinant HPIV2.

219. The method of claim 218, wherein said polynucleotide insertion specifies an attenuation phenotype of the recombinant HPIV2 which exhibits at least a 10-to 100-fold decrease in replication in the upper and/or lower respiratory tract.

220. The method of claim 183, which elicits a polyspecific immune response in the subject against multiple HPIVs.

221. The method of claim 183, which elicits a polyspecific immune response against multiple HPIVs and/or against a HPIV and a non-PIV pathogen.

222. The method of claim 183, which elicits a polyspecific immune response against a HPIV and measles virus.

223. The method of claim 183, which elicits a polyspecific immune response against a HPIV and respiratory syncytial virus.

224. The method of claim 183, which elicits a polyspecific immune response against a human HPIV human metapneumovirus.

225. The method of claim 183, wherein a first, chimeric HPIV2 comprising a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s), and a second PIV, are administered sequentially or simultaneously to elicit a polyspecific immune response.

226. The method of claim 225, wherein the second PIV is a second, chimeric PIV comprising a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s).

227. The method of claim 225, wherein the first, chimeric PIV and second PIV are administered simultaneously in a mixture.

228. The method of claim 225, wherein the first, chimeric PIV and second PIV are antigenically distinct HPIVs.

229. The method of claim 225, wherein the first, chimeric PIV comprises a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of a different PIV.

230. The method of claim 225, wherein one or both of the first, chimeric PIV and second PIV incorporate one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of a non-PIV pathogen.

231. The method of claim 225, wherein the first and second chimeric PIVs incorporate one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of the same non-PIV pathogen.

232. A method for sequential immunization to stimulate the immune system of a mammalian subject to induce an immune response against multiple pathogens comprising administering to the subject an immunologically sufficient amount of a first HPIV and subsequently administering to the subject an immunologically sufficient amount of a second HPIV, wherein at least one of said first and second HPIVs comprises a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous gene(s) or

genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s) to form a chimeric HPIV1 genome or antigenome.

233. The method for sequential immunization of claim 232, wherein said first HPIV is a chimeric HPIV2 virus.

234. The method for sequential immunization of claim 233, wherein said chimeric HPIV2 virus expresses one or more antigenic determinant(s) of HPIV3.

235. The method for sequential immunization of claim 232, wherein said chimeric HPIV2 virus expresses one or more antigenic determinant(s) of a respiratory syncytial virus.

236. The method for sequential immunization of claim 232, wherein said chimeric HPIV2 virus expresses one or more antigenic determinant(s) of a measles virus.

237. The method for sequential immunization of claim 232, wherein said second HPIV is a chimeric HPIV2 virus.

238. The method for sequential immunization of claim 237, wherein said chimeric HPIV2 virus expresses one or more antigenic determinant(s) of HPIV3.

239. The method for sequential immunization of claim 237, wherein said chimeric HPIV2 virus expresses one or more antigenic determinant(s) of HPIV1.

240. The method for sequential immunization of claim 237, wherein said chimeric HPIV2 virus expresses one or more antigenic determinant(s) of a respiratory syncytial virus.

241. The method for sequential immunization of claim 237, wherein said chimeric HPIV2 virus expresses one or more antigenic determinant(s) of a measles virus.

242. The method for sequential immunization of claim 232, wherein one of said first and second HPIVs is a chimeric HPIV2 virus capable of eliciting a polyspecific immune response in the subject against one or more HPIVs or against a HPIV and a non-PIV pathogen.

243. The method for sequential immunization of claim 232, wherein at least one of said first and second HPIVs is a chimeric HPIV2 virus capable of eliciting a polyspecific

immune response in the subject against one or more heterologous HPIVs or against a heterologous HPIV and a non-PIV pathogen.

244. The method for sequential immunization of claim 232, wherein following the first administration, the subject exhibits a primary antibody response against HPIV3 and/or a non-PIV pathogen, but not HPIV1 or HPIV2, and upon secondary immunization the subject is readily infected with the second HPIV and develops a primary antibody response to HPIV1 and/or HPIV2 and a high titered secondary antibody response against HPIV3 and/or the non-PIV pathogen.

245. The method for sequential immunization of claim 232, wherein the first HPIV elicits an immune response against HPIV3 and the second HPIV elicits an immune response against HPIV1 or HPIV2, and wherein one or both of the first and second HPIVs elicit an immune response against measles or RSV.

246. The method for sequential immunization of claim 232, wherein one or both of the first and second HPIVs expresses one or more antigenic determinan(s) of a non-PIV pathogen selected from measles virus, subgroup A and subgroup B respiratory syncytial viruses (RSVs), mumps virus, human papilloma viruses, type 1 and type 2 human immunodeficiency viruses, herpes simplex viruses, cytomegalovirus, rabies virus, human metapneumovirus, Epstein Barr virus, filoviruses, bunyaviruses, flaviviruses, alphaviruses and influenza viruses.

247. The method for sequential immunization of claim 232, wherein one or both of the first and second HPIVs incorporates one or more attenuating mutation(s).

248. The method for sequential immunization of claim 232, wherein one or both of the first and second HPIVs incorporates one or more mutation(s) identified in a biologically derived mutant PIV or other mutant nonsegmented negative stranded RNA virus.

249. The method for sequential immunization of claim 248, wherein one or both of the first and second HPIVs incorporates one or any combination of mutation(s) selected from mutations specifying amino acid substitution(s) or deletion(s) at corresponding target position(s) Tyr948, Ala998, Leu1566, Phe460 and/or Ser1724 in the HPIV2 L protein.

250. The method for sequential immunization of claim 232, wherein one or both of the first and second HPIVs incorporates at least one attenuating mutation stabilized by two or three nucleotide changes in a codon specifying the mutation.

251. The method for sequential immunization of claim 250, wherein said attenuating mutation comprises three nucleotide changes in a codon specifying an amino acid substitution or deletion at Ser1724 in the HPIV2 L protein.

252. The method for sequential immunization of claim 232, wherein the subject is a newborn to four month old human infant.

253. The method for sequential immunization of claim 232, wherein said first and second HPIVs are each formulated in a dose of 10^3 to 10^7 PFU.

254. The method for sequential immunization of claim 232, wherein said first and second HPIVs are each administered to the upper respiratory tract of the subject by spray, droplet or aerosol.

255. An isolated polynucleotide comprising a partial or complete, polyhexameric recombinant human parainfluenza virus type 2 (HPIV2) genome or antigenome modified by one or more attenuating mutations that are recombinantly introduced into said HPIV2 genome or antigenome.

256. The isolated polynucleotide of claim 255, wherein the HPIV2 genome or antigenome is recombinantly modified to incorporate one or more attenuating mutation(s) identified in a biologically derived mutant PIV strain or other mutant nonsegmented negative stranded RNA virus.

257. The isolated polynucleotide of claim 256, wherein the polynucleotide molecule encoding the recombinant HPIV2 genome or antigenome incorporates one or more mutation(s) of HPIV3 JS *cp45*.

258. The isolated polynucleotide of claim 257, wherein the recombinant HPIV2 genome or antigenome incorporates one or more attenuating mutation(s) selected from amino acid substitution(s) or deletion(s) at residues 948 and/or 1566 of the HPIV2 L polymerase.

259. The isolated polynucleotide of claim 255, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is respiratory syncytial virus (RSV).

260. The isolated polynucleotide of claim 259, wherein said attenuating mutation comprises an amino acid substitution or deletion at a corresponding target position Phe460 in the HPIV2 L protein.

261. The isolated polynucleotide of claim 255, wherein the heterologous, mutant nonsegmented negative stranded RNA virus is a bovine parainfluenza virus type 3 (BPIV3).

262. The isolated polynucleotide of claim 261, wherein said attenuating mutation comprises one or more amino acid substitution(s) or deletion(s) targeting at least Ser1724 in the HPIV2 L protein.

263. The isolated polynucleotide of claim 262, wherein said attenuating mutation comprises a two amino acid deletion at Ser1724-1725 in the HPIV2 L protein.

264. The isolated polynucleotide of claim 255, wherein the recombinant HPIV2 genome or antigenome incorporates at least one attenuating mutation stabilized by two or three nucleotide changes in a codon specifying the mutation.

265. The isolated polynucleotide of claim 255, wherein one or more gene(s) of the HPIV2 genome or antigenome is deleted in whole or in part or is modified by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters an amino acid specified by an initiation codon, or by introduction of one or more stop codons in an open reading frame (ORF) of the gene.

266. The isolated polynucleotide of claim 255, wherein the HPIV2 genome or antigenome is modified by a partial or complete deletion of a PIV2 V open reading frame (ORF) or one or more nucleotide change(s) that reduces or ablates expression of said V ORF.

267. The isolated polynucleotide of claim 255, wherein the HPIV2 genome or antigenome is modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

268. The isolated polynucleotide of claim 255, wherein the HPIV2 genome or antigenome is modified to comprise a partial or complete HPIV2 vector genome or antigenome, wherein said vector genome or antigenome is combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s) to form a chimeric HPIV1 genome or antigenome.

269. The isolated polynucleotide of claim 268, wherein one or more gene(s) or genome segment(s) encoding one or more antigenic determinant(s) selected from HPIV1 and HPIV3 HN and F glycoproteins, and antigenic domains, fragments and epitopes thereof, is/are added to or substituted within the partial or complete HPIV2 vector genome or antigenome.

270. The isolated polynucleotide of claim 268, wherein the heterologous pathogen is selected from measles virus, subgroup A and subgroup B respiratory syncytial viruses, mumps virus, human papilloma viruses, type 1 and type 2 human immunodeficiency viruses, herpes simplex viruses, cytomegalovirus, rabies virus, Epstein Barr virus, filoviruses, bunyaviruses, flaviviruses, alphaviruses, human metapneumoviruses, and influenza viruses.

271. The isolated polynucleotide of claim 268, wherein the HPIV2 vector genome or antigenome is modified to encode a chimeric glycoprotein incorporating one or more antigenic domains, fragments, or epitopes from a second, antigenically distinct PIV to form the chimeric genome or antigenome.

272. The isolated polynucleotide of claim 268, wherein the chimeric HPIV2 genome or antigenome is recombinantly modified by introduction of one or more attenuating mutations identified in a biologically derived mutant PIV or other mutant nonsegmented negative stranded RNA virus.

273. The isolated polynucleotide of claim 272, wherein the chimeric HPIV2 genome or antigenome is recombinantly modified to incorporate one or any combination of mutation(s) selected from mutations specifying amino acid substitution(s) or deletion(s) at corresponding target position(s) Tyr948, Ala998, Leu1566, Phe460 and/or Ser1724 in the HPIV2 L protein.

274. The isolated polynucleotide of claim 268, wherein the chimeric HPIV2 genome or antigenome is further modified such that one or more HPIV2 gene(s) is/are deleted in whole or in part or expression of the gene(s) is reduced or ablated by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters a translation start site, by introduction of one or more stop codons in an open reading frame (ORF) of the gene, or by a mutation in a transcription signal.

275. The isolated polynucleotide of claim 268, wherein the chimeric HPIV2 genome or antigenome is further modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

276. The isolated polynucleotide of claim 268, wherein the chimeric HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous genes or genome segments from a bovine parainfluenza type 3 virus (BPIV3) to form a human-bovine chimeric HPIV2 genome or antigenome.

277. The isolated polynucleotide of claim 268, wherein the chimeric HPIV2 genome or antigenome incorporates a polynucleotide insertion of between 150 nucleotides (nts) and 4,000 nucleotides in length in a non-coding region (NCR) of the genome or antigenome or as a separate gene unit (GU), said polynucleotide insertion lacking a complete open reading frame (ORF) and specifying an attenuated phenotype in said recombinant HPIV2.

278. An expression vector comprising an operably linked transcriptional promoter, a polynucleotide sequence comprising a partial or complete, polyhexameric recombinant human parainfluenza virus type 2 (HPIV2) genome or antigenome modified by one or more attenuating mutations that are recombinantly introduced into said HPIV2 genome or antigenome, and a transcriptional terminator.

279. The expression vector of claim 278, wherein the HPIV2 genome or antigenome is recombinantly modified to incorporate one or more attenuating mutation(s) identified in a biologically derived mutant PIV strain or other mutant nonsegmented negative stranded RNA virus.

280. The expression vector of claim 279, wherein the HPIV2 genome or antigenome is recombinantly modified to incorporate one or any combination of mutation(s) selected from mutations specifying amino acid substitution(s) at corresponding target position(s) Tyr948, Ala998, Leu1566, Phe460 and/or Ser1724 in the HPIV2 L protein.

281. The expression vector of claim 278, wherein one or more gene(s) of the HPIV2 genome or antigenome is deleted in whole or in part or is modified by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters an amino acid specified by an initiation codon, or by introduction of one or more stop codons in an open reading frame (ORF) of the gene.

282. The expression vector of claim 281, wherein the HPIV2 genome or antigenome is modified by a partial or complete deletion of a HPIV2 V open reading frame (ORF) or by one or more nucleotide change(s) that reduces or ablates expression of said V ORF.

283. The expression vector of claim 278, wherein the HPIV2 genome or antigenome is modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

284. The expression vector of claim 278, wherein the HPIV2 genome or antigenome is modified to comprise a partial or complete HPIV2 vector genome or antigenome, wherein said vector genome or antigenome is combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of one or more heterologous pathogen(s) to form a chimeric HPIV2 genome or antigenome.

285. The expression vector of claim 284, wherein one or more gene(s) or genome segment(s) encoding one or more antigenic determinant(s) selected from HPIV1 and HPIV3 HN and F glycoproteins, and antigenic domains, fragments and epitopes thereof, is/are added to or substituted within the partial or complete HPIV2 vector genome or antigenome.

286. The expression vector of claim 284, wherein the heterologous pathogen is selected from measles virus, subgroup A and subgroup B respiratory syncytial viruses, mumps virus, human papilloma viruses, type 1 and type 2 human immunodeficiency viruses,

herpes simplex viruses, cytomegalovirus, rabies virus, Epstein Barr virus, filoviruses, bunyaviruses, flaviviruses, alphaviruses, human metapneumoviruses, and influenza viruses.

287. The expression vector of claim 284, wherein the HPIV2 vector genome or antigenome is modified to encode a chimeric glycoprotein incorporating one or more antigenic domains, fragments, or epitopes from a second, antigenically distinct PIV to form the chimeric genome or antigenome.

288. The expression vector of claim 284, wherein the chimeric HPIV2 genome or antigenome is recombinantly modified by introduction of one or more attenuating mutations identified in a biologically derived mutant PIV or other mutant nonsegmented negative stranded RNA virus.

289. The expression vector of claim 284, wherein the chimeric HPIV2 genome or antigenome is recombinantly modified to incorporate one or any combination of mutation(s) selected from mutations specifying amino acid substitution(s) at corresponding target position(s) Tyr948, Ala998, Leu1566, Phe460 and/or Ser1724 in the HPIV2 L protein.

290. The expression vector of claim 284, wherein the chimeric HPIV2 genome or antigenome is modified such that one or more HPIV2 gene(s) is/are deleted in whole or in part or expression of the gene(s) is reduced or ablated by a mutation in an RNA editing site, by a frameshift mutation, by a mutation that alters a translation start site, by introduction of one or more stop codons in an open reading frame (ORF) of the gene, or by a mutation in a transcription signal.

291. The expression vector of claim 284, wherein the chimeric HPIV2 genome or antigenome is modified by a partial or complete deletion of a HPIV2 V open reading frame (ORF) or one or more nucleotide change(s) that reduces or ablates expression of said HPIV2 V ORF.

292. The expression vector of claim 284, wherein the chimeric HPIV2 genome or antigenome is modified to encode a non-PIV molecule selected from a cytokine, a T-helper epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting an immune response in a mammalian host.

293. The expression vector of claim 284, wherein the chimeric HPIV2 genome or antigenome comprises a partial or complete HPIV2 vector genome or antigenome combined with one or more heterologous genes or genome segments from a bovine parainfluenza virus type 3 virus (BPIV3) to form a human-bovine chimeric HPIV2 genome or antigenome.

294. The expression vector of claim 284, wherein the HPIV2 genome or antigenome incorporates a polynucleotide insertion of between 150 nucleotides (nts) and 4,000 nucleotides in length in a non-coding region (NCR) of the genome or antigenome or as a separate gene unit (GU), said polynucleotide insertion lacking a complete open reading frame (ORF) and specifying an attenuated phenotype in said recombinant HPIV2.